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THE CONSTITUENTS
OF
COMMERCIAL CHRYSAROBIN

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XXXVII.—*The Constituents of Commercial Chrysarobin.*

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Chrysarobin is a product obtained from Araroba or Goa powder (a deposit found in the wood of *Andira Araroba*, Aguiar) by extraction with certain solvents, such as chloroform or benzene, evaporating the extract to dryness, and powdering the residue. It has been the subject of several chemical investigations, the most important of which is that of Jowett and Potter (Trans., 1902, **81**, 1575), who fully reviewed the literature on the subject. Since the work of the above-mentioned authors a communication has appeared by Oesterle and Johann (*Arch. Pharm.*, 1910, **248**, 476), in which they showed that emodin monomethyl ether could be obtained from chrysarobin, and suggested that it was contained in the "dichrysarobin methyl ether" described by Jowett and Potter. Inasmuch as the results of no two of the previous investigations have shown any material agreement, it was deemed desirable again to examine the subject.

The results of the present investigation, which are summarised at the end of this paper, have shown that chrysarobin is a variable product, and more complicated in its nature than was heretofore supposed. Two new compounds have been isolated from it, one of which occurs in considerable proportions, and certain products previously described as individual substances have been shown to be mixtures.

Throughout the course of the work considerable difficulty has repeatedly been met with owing to the great tendency of the constituents of the chrysarobin to crystallise together, yielding products of apparent homogeneity and constancy of composition. In most cases, therefore, it was necessary, in addition to fractional crystallisation, to employ other means for the isolation of the substances described.

Experimental.

I.—*Examination of Araroba Powder.*

For the purpose of the present investigation it was thought advisable, in the first place, to make a complete examination of Araroba or Goa powder, the natural product from which chrysarobin is obtained. The material employed consisted of a good quality of the drug, which had been obtained from a trustworthy source.

As a preliminary experiment, 10 grams of the Araroba powder were extracted successively in a Soxhlet apparatus with various solvents, when the following amounts of extract, dried at 110°, were obtained:

Petroleum (b. p. 35—50°)	extracted	3·73 grams	=	37·3	per cent.
Ether	,,	1·28 ,,	=	12·8	,,
Chloroform	,,	0·27 ,,	=	2·7	,,
Ethyl acetate	,,	0·14 ,,	=	1·4	,,
Alcohol	,,	0·33 ,,	=	3·3	,,
Total	=	5·75 grams	=	57·5	per cent.

The portion of the material left undissolved by this treatment (42·5 per cent.) consisted of dark-coloured, gummy matter and inorganic substances.

A quantity (1 kilogram) of the Araroba powder was completely extracted by continuous percolation with hot alcohol, and from the resulting extract the greater part of the alcohol was removed. The residue was then mixed with water, and distilled in a current of steam, but nothing appreciable was removed by this treatment.

The mixture remaining in the distillation flask consisted of a yellowish-brown, finely divided solid and a brown, aqueous liquid. These products were separated by filtration, and the solid washed and dried, after which it weighed 510 grams. The aqueous filtrate and washings were thoroughly examined, but they yielded only a trace of emodin monomethyl ether (m. p. 197°), some brown, amorphous material, and a small amount of a sugar which gave *d*-phenylglucosazone (m. p. 209°). No tannin was present.

The above-mentioned solid, which had been separated from the aqueous liquid, was mixed with purified sawdust, and submitted to a very thorough extraction in a large Soxhlet apparatus with petroleum (b. p. 35—50°), ether, chloroform, ethyl acetate, and alcohol.

Examination of the Petroleum Extract.

The petroleum extract of the solid consisted, for the most part, of a very sparingly soluble, orange-red powder, which amounted to 420 grams. The petroleum solution was decanted from it, and evaporated, when 2 grams of residue were obtained. This product on examination was found to consist chiefly of the anthraquinone derivatives subsequently to be described, but it also yielded a small amount of the higher fatty acids, together with a trace of a substance which appeared to be a hydrocarbon.

Isolation of Emodin, $C_{15}H_{10}O_5$.

The above-mentioned, orange-red coloured solid, which was very sparingly soluble in petroleum, was dissolved in 2 litres of chloroform, and the resulting liquid extracted successively with aqueous ammonium carbonate and sodium carbonate. During these operations appreciable quantities of a nearly black, finely divided solid separated, which gave rise to the formation of troublesome emulsions. Nothing crystalline could be obtained from the suspended solid matter, and no precipitate was formed on acidifying the filtered liquid obtained after shaking with the first-mentioned alkali. When, however, the filtered alkaline liquid obtained after shaking with aqueous sodium carbonate was acidified, a quantity (about 0·8 gram) of an orange-coloured powder separated. This was collected and recrystallised from dilute pyridine, when it formed orange-coloured needles (m. p. 252°), and was identified as emodin.* (Found, C = 66·5; H = 3·9. Calc., C = 66·7; H = 3·7 per cent.) The identity of this substance was further confirmed by its conversion into triacetylemodin, which formed slender, pale yellow prisms, melting at 194°.

Emodintridiphenylurethane, $CH_3\cdot C_{14}H_4O_5(CO\cdot NPh_2)_3$.—With the endeavour to form derivatives of the new compounds subsequently described, experiments were conducted with the employment of diphenylcarbamyl chloride. Although these experiments proved unsuccessful as regards the new compounds mentioned, it was found in a preliminary experiment that emodin readily yielded a *tridiphenylurethane*, a compound which has not previously been described.

A quantity (0·5 gram) of emodin was dissolved in pyridine, and the solution heated with 1·4 grams of diphenylcarbamyl chloride according to Herzog's method (*Ber.*, 1907, **40**, 1831). The resulting tridiphenylurethane separates from a mixture of alcohol and pyridine in small, pale yellow, flattened needles melting at 193°:

0·1103 gave 0·3048 CO_2 and 0·0434 H_2O. C = 75·4; H = 4·4.

$C_{54}H_{37}O_8N_3$ requires C = 75·7; H = 4·3 per cent.

Emodintridiphenylurethane is readily soluble in chloroform, benzene, or pyridine, and moderately soluble in ethyl acetate, but it dissolves only sparingly in alcohol.

Isolation of Chrysophanol,† $C_{15}H_{10}O_4$.

The original chloroform solution, from which the emodin had been removed, as above described, was evaporated, and the residue heated with a quantity of ethyl acetate. The hot mixture was then filtered, when a quantity (25 grams) of a yellow, crystalline powder was obtained. This product was found to consist of a mixture of substances, and it was therefore sought to effect a preliminary separation by fractional extraction with aqueous potassium hydroxide. Jowett and Potter (*loc. cit.*), however, obtained from commercial chrysarobin, chrysophanolanthranol ("chrysarobin"*), which, when dissolved in aqueous alkalis, is rapidly oxidised to chrysophanol. With the object, therefore, of ascertaining whether free chrysophanol was also present in the drug, the behaviour of the pure anthranol prepared by the above-mentioned investigators towards aqueous alkali of various concentrations was examined. It was then found that chrysophanolanthranol was much less acidic than the corresponding anthraquinone derivative, being only slowly removed from its solution in chloroform by a 5 per cent. solution of potassium hydroxide, whilst it was quite unaffected by a 2 per cent. solution. Chrysophanol, on the other hand, may be extracted from its solution in chloroform by a 1·5 per cent. solution of the alkali. The above-mentioned solid, which was sparingly soluble in ethyl acetate, was therefore dissolved in chloroform, and the solution shaken with ten successive portions of aqueous potassium hydroxide (1·5 per cent.). The yellow powder which was precipitated on acidifying these alkaline extracts was heated with acetic anhydride, and the resulting acetylated product fractionally crystallised. The greater part of the material was then found to be diacetylchrysophanol (m. p. 203°). The latter was hydrolysed by heating with hydrochloric acid in aqueous acetic acid solution, when chrysophanol was obtained in deep orange-coloured leaflets melting at 191°. (Found, C=70·8; H=4·1. Calc., C=70·9; H=3·9 per cent.) It is thus evident that chrysophanol is a constituent of Araroba powder, and consequently of chrysarobin. Attfield (*Pharm. J.*, 1875, [iii], **5**, 721) stated that chrysarobin consisted chiefly of "chrysophanic acid," whilst Hesse (*Annalen*, 1899, **309**, 32) denied that the latter was present, and Jowett and Potter (*loc. cit.*) did not isolate any of it.

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* Since emodinanthranol is dissolved and oxidised when shaken with aqueous sodium carbonate, there is no proof that the emodin obtained from Araroba powder did not occur partly, or possibly wholly, as the corresponding anthranol.

† The name chrysophanic acid was originally applied to a product which is now known to have consisted of a mixture of a dihydroxymethylanthraquinone, $C_{15}H_{10}O_4$, and emodin monomethyl ether. More recently, it has been applied to the former

The chloroform solution, from which the crude chrysophanol had been removed as above described, was evaporated, when the residue was found to consist of a mixture of substances which could not

compound, which was first obtained in a state of purity by Jowett and Potter (*loc. cit.*). Since, however, the dihydroxymethylanthraquinone in question is not an acid, it is much more appropriately termed chrysophanol (compare Tschirch *Arch. Pharm.*, 1912, **250**, 27).

* Since the name chrysarobin is applied to the commercial product obtained by the extraction of Araroba powder, it is considered inadvisable also to employ it as a designation for chrysophanolanthranol, as was done by Jowett and Potter (*loc. cit.*).

readily be separated by crystallisation. With the endeavour to isolate chrysophanolanthranol from this mixture, the entire material was acetylated, and the resulting product fractionally crystallised. The only compound, however, which could be separated in a state of purity was a bright yellow-coloured substance melting at 206°, of which a small amount was isolated:

0·0916 gave 0·2226 CO_2 and 0·0372 H_2O. C = 66·3; H = 4·5.

$C_{16}H_{10}O_4(OH)\cdot CO\cdot CH_3$ requires C = 66·3; H = 4·3 per cent.

This substance is thus seen to be a *monoacetyl* derivative of emodin monomethyl ether. It is removed from its solution in chloroform by dilute aqueous potassium hydroxide, and on further acetylation yields diacetylemodin monomethyl ether (m. p. 189°).

Isolation of Emodin Monomethyl Ether.

The hot ethyl acetate filtrate from the above-described solid which yielded the chrysophanol deposited on cooling about 1 gram of a crystalline substance. The latter after repeated crystallisation from ethyl acetate yielded deep orange-coloured leaflets melting at 200°, which proved to be emodin monomethyl ether. (Found, C = 67·4; H = 4·4. Calc., C = 67·6; H = 4·2 per cent.) This monomethyl ether of emodin was identical with the compound of similar nature obtained by the present authors from *Rumex Ecklonianus* (Trans., 1910, **97**, 1) and from rhubarb (Trans., 1911, **99**, 946). Its identity was further confirmed by the preparation of its diacetyl derivative, which melted at 189°, and by its hydrolysis to emodin by means of concentrated sulphuric acid.

Isolation of a New Compound, Ararobinol, $C_{23}H_{16}O_5$.

The original ethyl acetate liquid, from which the products that yielded chrysophanol and emodin monomethyl ether had been separated as above described, was evaporated to a low bulk, and about 1 litre of ether added. This precipitated a quantity (5·5 grams) of a product which was found to consist chiefly of chrysophanol, together with a small amount of emodin monomethyl ether. The ethereal filtrate from these compounds was first examined for the presence of aloe-emodin by extraction with a 0·5 per cent. solution of aqueous potassium hydroxide, but with a negative result. It was then shaken with eight successive portions of 1·5 per cent. aqueous potassium hydroxide, which treatment removed further quantities of chrysophanol and emodin monomethyl ether. The ethereal liquid was then shaken with two successive portions of 5 per cent. aqueous potassium hydroxide, when a quantity (0·2 gram) of a product was removed, which differed in appearance from the material removed by the weaker alkali solution. This product was crystallised from a mixture of ethyl acetate and glacial acetic acid, when yellow, flattened crystals were obtained, which blackened and decomposed at about 225°, but possessed no definite melting point. A further amount (about 1 gram) of the same substance was obtained on crystallising the residue left on evaporating the ethereal liquid. It was not altered by further crystallisation, and possessed all the attributes of homogeneity:

0·1109 gave 0·3016 CO_2 and 0·0468 H_2O. C=74·2; H=4·7.
0·0896 „ 0·2434 CO_2 „ 0·0380 H_2O. C=74·1; H=4·7.
$C_{23}H_{16}O_5$ requires C=74·2; H=4·3 per cent.

This substance does not agree in its composition and properties with any compound previously described, and it is therefore proposed to designate it *ararobinol*, with reference to the name of the material from which it was obtained.

Ararobinol is readily soluble in glacial acetic acid, but somewhat sparingly so in the other usual solvents. It is not affected by 1·5 per cent. aqueous potassium hydroxide, but dissolves fairly readily in a 10 per cent. solution of the alkali, giving a yellow liquid which does not darken appreciably on exposure to the air. When ararobinol is treated with concentrated sulphuric acid a most striking and characteristic colour reaction is produced. If the merest trace of the substance be treated with sulphuric acid, it immediately acquires an orange colour. Then, on slightly agitating the liquid, streaks of an intense blue colour appear, intermingled with the original orange colour; the blue colour then suffuses the whole liquid, which subsequently assumes a green colour, and finally a dull grey tint.

Triacetylararobinol, $C_{23}H_{13}O_5(CO\cdot CH_3)_3$.—A quantity of ararobinol was heated with acetic anhydride in the presence of a trace of *d*-camphorsulphonic acid. The greater part of the anhydride was then evaporated, and the residue diluted with ether, when nearly colourless, flattened prisms separated:

0·0786 gave 0·2006 CO_2 and 0·0342 H_2O. C=69·6; H=4·8.
$C_{29}H_{22}O_8$ requires C=69·9; H=4·4 per cent.

Triacetylararobinol, like its parent substance, decomposes at about 225°, and yields the above-described colour reaction on treatment with concentrated sulphuric acid.

Dihydroararobinol, $C_{23}H_{18}O_5$.—A quantity of ararobinol was heated for some hours with hydriodic acid (D 1·7), to which some glacial acetic acid had been added, but no methyl iodide was evolved. It was evident, however, that the compound had undergone some change. The contents of the flask were diluted, and the crystalline solid collected and recrystallised from glacial acetic acid. Small, greenish-yellow, rectangular plates were then obtained, which gradually blackened and decomposed at about 180°:

0·1004 gave 0·2703 CO_2 and 0·0458 H_2O. C = 73·4; H = 5·1.

$C_{23}H_{18}O_5$ requires C = 73·8; H = 4·8 per cent.

This substance is thus seen to be *dihydroararobinol.* It is sparingly soluble in the usual organic solvents, and is practically insoluble in aqueous potassium hydroxide of any concentration. It dissolves in concentrated sulphuric acid, giving an orange colour, which slowly darkens.

Oxidation of Ararobinol.—A quantity of ararobinol and an equal weight of chromic acid were dissolved in slightly diluted acetic acid, and the mixture boiled for one hour. The liquid was then poured into water and extracted with chloroform, when chrysophanol was obtained, but not in quantitative yield. The latter melted at 191°, and its identity was confirmed by the preparation of its acetyl derivative (m. p. 203°).

Isolation of Chrysophanolanthranol, $C_{15}H_{12}O_3$.

Jowett and Potter (*loc. cit.*) obtained from the petroleum extract of commercial chrysarobin by a very tedious fractional crystallisation a small amount of chrysophanolanthranol ("chrysarobin"). They also showed that the same compound could be obtained much more readily after heating the above-mentioned petroleum extract with hydriodic acid. During the foregoing experiments no chrysophanolanthranol was isolated, but indications of its presence were obtained, particularly in the feebly acidic product which was acetylated as previously described. A special search for the anthranol in question was therefore made with the employment of a further quantity of Araroba powder. A quantity (500 grams) of Araroba powder was thoroughly extracted in a Soxhlet apparatus with light petroleum, the solvent removed from the extract, and the residue digested with a limited amount of ethyl acetate, cooled, and filtered. The yellow solid so obtained was dissolved in chloroform, deprived of emodin by means of aqueous sodium carbonate, and then extracted with eighteen successive portions of a 1·5 per cent. aqueous solution of potassium hydroxide. This treatment removed a considerable amount of a mixture of chrysophanol and emodin monomethyl ether. The chloroform solution was then shaken several times with a 2 per cent. solution of the alkali to remove the last traces of the above-mentioned anthraquinone derivatives, washed, and evaporated. The residue was then fractionally crystallised many times from glacial acetic acid, when a product was obtained in yellow leaflets, which appeared to be homogeneous:

0·1000 gave 0·2746 CO_2 and 0·0458 H_2O. C=74·9; H=5·1.
$C_{15}H_{12}O_3$ requires C=75·0; H=5·0 per cent.

This product melted at 199°, and a mixture of it with pure chrysophanolanthranol prepared by Jowett and Potter by the action of hydriodic acid on chrysarobin melted at the same temperature. It exhibited all the properties of chrysophanolanthranol as described by the above-mentioned authors, but notwithstanding this fact and the excellent result it gave on analysis, it was found to be not quite pure. This was demonstrated in the following way: A quantity of the product melting at 199° was dissolved in acetic acid, chromic acid added, and the mixture heated to boiling and then poured into water. This treatment was found to convert all chrysophanolanthranol into its parent compound, but it was not a sufficiently vigorous oxidation to attack ararobinol. On working up the product it was found to consist, for the most part, of chrysophanol, but it also yielded a small amount of ararobinol. It was thus proved that chrysophanolanthranol, as obtained by us from Araroba powder, was not quite pure, and, moreover, it was found impossible to obtain a specimen of it by crystallisation alone which was free from ararobinol.

Examination of the Ethereal Extract.

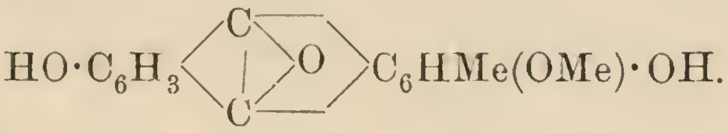
The ethereal extract of the original solid (p. 291) weighed 40 grams. It was heated with chloroform, and a small quantity of undissolved material removed. The latter was found to be the *monomethyl ether* of *dehydroemodinanthranol*, subsequently described. The chloroform solution was extracted successively with aqueous ammonium carbonate and sodium carbonate, when troublesome emulsions, caused by the separation of a fine, black powder, were formed at each operation. The solid causing these emulsions yielded nothing crystalline, as was also the case with the ammonium carbonate solution, but on acidifying the alkaline liquid obtained by extraction with sodium carbonate about 2·5 grams of emodin were obtained. The chloroform solution was then extracted with eleven successive portions of a 2 per cent. aqueous solution of potassium hydroxide, which deprived it of emodin monomethyl ether and chrysophanol, when it was washed and evaporated.

Isolation of the Monomethyl Ether of Dehydroemodinanthranol.

The yellow residue (about 8 grams) obtained on evaporating the chloroform solution as above described was digested with 800 c.c. of boiling glacial acetic acid. A quantity (0·5 gram) of material then remained undissolved, and was removed. A further amount of the same sparingly soluble compound was obtained on fractionally crystallising the material contained in the glacial acetic acid filtrate. The total amount of the compound isolated in this place was 2 grams, and it was found to be identical with the small amount of material sparingly soluble in chloroform which had been separated as above described. The compound was purified by crystallisation from a large volume of hot, glacial acetic acid, when long, pale yellow needles were obtained, which decomposed and melted at 265°:

0·0954 gave 0·2504 CO_2 and 0·0410 H_2O. C = 71·6; H = 4·8.
0·1013 „ 0·2660 CO_2 „ 0·0434 H_2O. C = 71·6; H = 4·8.
$C_{16}H_{12}O_4$ requires C = 71·6; H = 4·5 per cent.

This substance does not agree in its composition and properties with any compound previously described, and, as shown below, it was the anthranol of emodin monomethyl ether less 2 atoms of hydrogen. It is therefore the *monomethyl ether* of *dehydroemodinanthranol.* It was found to oxidise with markedly greater difficulty than the anthranols, and it therefore probably differs from the monomethyl ether of emodinanthranol by the loss of two atoms of hydrogen in the characteristic anthranol grouping. It may therefore be represented as follows:



$$HO\cdot C_6H_3\left\langle\begin{matrix}C\\ |\\ C\end{matrix}\right\rangle O \rangle C_6HMe(OMe)\cdot OH.$$

The monomethyl ether of dehydroemodinanthranol is very sparingly soluble, or insoluble, in the usual solvents, but is moderately soluble in warm tetrachloroethane. Its solution in organic solvents darkens somewhat on keeping, owing to the formation of an amorphous, sparingly soluble, dark-coloured decomposition product, and it is doubtless due to this property that emulsions caused by the separation of a black, amorphous powder were so frequently met with throughout the course of this work.

Action of Hydriodic Acid on the Monomethyl Ether of Dehydroemodinanthranol.—A determination of the methoxyl in the monomethyl ether of dehydroemodinanthranol was made by Perkin's modification of Zeisel's method, with the following result; it was necessary, however, to add glacial acetic acid to the hydriodic acid employed, as otherwise the methyl iodide was evolved extremely slowly:

0·2972 gave 0·2387 AgI. OMe = 10·6.
$C_{15}H_9O_3{\cdot}OMe$ requires OMe = 11·6 per cent.*

After the determination of the methoxyl, as above described, the flask containing the hydriodic and acetic acids was observed to contain also a quantity of a well-crystallised compound. The latter was collected, and recrystallised from a mixture of glacial acetic acid and ethyl acetate, when it formed small, yellow leaflets, which decomposed at about 255°:

0·1065 gave 0·2748 CO_2 and 0·0456 H_2O. C = 70·4; H = 4·8.
$C_{15}H_{12}O_4$ requires C = 70·3; H = 4·7 per cent.

On oxidation this substance yielded emodin (m. p. 252°), which was identified by the formation of its triacetyl derivative, and it thus appeared to be emodinanthranol. The latter compound, however, has been prepared by Krasowsky (*J. Russ. Phys. Chem. Soc.*, 1908, **40**, 1510), who described it as forming colourless crystals melting at 280°. In order, therefore, to confirm the identity of our compound (decomp. 255°) with emodinanthranol, a quantity of emodin (from rhubarb) was reduced with hydriodic acid, when a yellow-coloured anthranol was obtained. It decomposed at 255°, and was identical in all respects with the above-described compound.

Oxidation of the Monomethyl Ether of Dehydroemodinanthranol.—The monomethyl ether of dehydroemodinanthranol was not appreciably affected by a treatment with chromic acid sufficiently vigorous to convert an anthranol into the corresponding anthraquinone, but when subjected to a more energetic and prolonged treatment it underwent change.

A quantity (0·2 gram) of the dehydroanthranol, together with 0·3 gram of chromic acid, was dissolved in glacial acetic acid, and the mixture boiled for three hours. On working up the product a practically quantitative yield of emodin monomethyl ether (m. p. 200°) was obtained.

No crystalline acetyl derivative could be obtained from the monomethyl ether of dehydroemodinanthranol, and an attempt to prepare a diphenylurethane from it by heating with diphenylcarbamyl chloride in pyridine solution resulted only in the production of an intensely green liquid, from which nothing crystalline could be isolated.

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* The somewhat low result yielded by this determination is due to the great difficulty with which the methyl iodide was evolved from the compound under examination. This was proved by the fact that the crude emodinanthranol resulting from the reaction was found also to contain a small amount of emodin monomethyl ether anthranol.

The chloroform, ethyl acetate, and alcohol extracts of the original solid (p. 291) amounted to 34, 1, and 3 grams respectively. They all consisted of black, amorphous products, and nothing crystalline could be obtained from any of them.

II.—*Examination of Commercial Samples of Chrysarobin.*

Three commercial samples of chrysarobin, which may be designated as *A*, *B*, and *C* respectively, were obtained from trustworthy sources; sample *A* came from the same firm as had supplied the Araroba powder, the examination of which has just been described.

It was found that a preliminary idea of the nature of the product might be obtained by estimating quantitatively the amount of oxygen absorbed by an alkaline solution of the material. Chrysophanolanthranol, when air is passed through its solution in alkali, absorbs practically the theoretical amount of oxygen (13·3 per cent.) in about two hours. The monomethyl ether of dehydroemodinanthranol, however, is oxidised much more slowly under similar conditions, and ararobinol also appears very slowly to absorb oxygen. Known weights of the various products were therefore dissolved in a weighed amount of aqueous potassium hydroxide in a suitable apparatus, and air passed through the mixture, the necessary precautions to ensure a quantitative determination being taken. The following results were then obtained:

Material.	Weight taken.	Oxygen absorbed during first two hours.	Oxygen absorbed during fifteen hours.
Sample *A*	0·9022	6·7 per cent.	11·0 per cent.
,, *B*	0·8816	7·4 ,,	10·7 ,,
,, *C*	0·9596	5·1 ,,	10·1 ,,
Petroleum extract of Araroba powder.........	1·9130	6·9 ,,	—
Chrysophanolanthranol .	0·2340	12·8 ,,	—

From these figures it would appear that none of the commercial products consisted essentially of anthranols or similar substances, as has been indicated by the work of previous investigators.

A quantity (100 grams) of each of the samples, *A*, *B*, and *C*, was then mixed with purified sawdust, and submitted to prolonged extraction in a Soxhlet apparatus with petroleum (b. p. 35—40°), ether, and chloroform, when the entire amount of the material was removed. Although the extraction with petroleum was continued for a number of weeks, no sharp separation was effected, for it was found that the same compounds were, in each case, present in both the petroleum and ether extracts, but in different proportions. The following were the amounts of extracts obtained:

Material.	Petroleum extract.	Ether extract.	Chloroform extract.*
Sample *A*	54 grams	42 grams	0·5 gram
,, *B*	45 ,,	52 ,,	0·5 ,,
,, *C*	24 ,,	74 ,,	nil

* It was found that if the ether extraction were not carried to finality, subsequent extraction with chloroform yielded a product from which pure monomethyl ether of dehydroemodinanthranol could be obtained by a single crystallisation from acetic acid.

The petroleum and ether extracts of these samples were then separately examined according to the scheme outlined below, the chloroform extracts consisting only of amorphous products. It was necessary, however, to modify the procedure somewhat, according to the nature of the different extracts, as the products varied appreciably in their composition.

The extract to be examined was dissolved in chloroform, and the resulting solution deprived of emodin by extraction with aqueous sodium carbonate. The chrysophanol and emodin monomethyl ether were then completely removed by many extractions with 1·5 per cent. aqueous potassium hydroxide. The chloroform solution was then washed and evaporated, and the residue boiled with glacial acetic acid, when a quantity of undissolved monomethyl ether of dehydroemodinanthranol was removed by filtration from the hot liquid. The material contained in the filtrate yielded on fractional crystallisation a further quantity of the last-mentioned compound, together with ararobinol and crude chrysophanolanthranol. The anthranol, however, could never be isolated in a state of purity, and a certain proportion of the material always remained as an inseparable mixture of the various compounds described. An estimate of the amount of chrysophanolanthranol present was readily obtained by extracting the crude product from its solution in chloroform by a sufficiently concentrated aqueous alkali, when oxidation also occurred. The amount of chrysophanol formed could then readily be ascertained. In carrying out this experiment, however, it was found that some emodin monomethyl ether was also formed, thus proving the presence of a small amount of the anthranol of this compound.

The approximate composition of the three commercial samples examined is indicated on p. 302.

The bearing of the results of the present examination on the work of earlier investigators should now be considered.

The original statement by Attfield (*loc. cit.*) that chrysarobin contained chrysophanic acid, identical with that obtained from rhubarb by Schlössberger and Döpping, is strictly correct, since the latter product was really a mixture of chrysophanol and emodin monomethyl ether similar to that occurring in chrysarobin (compare Trans., 1911, **99**, 946). The amount of "chrysophanic acid" indicated by Attfield to be contained in chrysarobin was, however, much greater than that actually present. Jowett and Potter (*loc. cit.*), who fully considered the work of Liebermann and Seidler (*Ber.*, 1878, **11**, 1603), of Liebermann (*ibid.*, 1881, **21**, 437; *Annalen*, 1882, **212**, 41), and of Hesse (*ibid.*, 1899, **309**, 32), stated that they had isolated from commercial chrysarobin the following substances: Chrysophanolanthranol ("chrysarobin"), "dichrysarobin," "dichrysarobin methyl ether," and a substance, $C_{17}H_{14}O_4$. In the present investigation we have confirmed the statement regarding the presence of the anthranol, but could obtain none of the other three compounds. With regard to the substance $C_{17}H_{14}O_4$, we can only say that no compound of this composition could be detected by us in any of the products examined. With regard to "dichrysarobin" and its "methyl ether," however, the experience gained during the present work led us to doubt their homogeneity; for instance, during this investigation a product was obtained which appeared to possess all the attributes of homogeneity, and which agreed approximately in its composition and properties with the "dichrysarobin methyl ether" of Jowett and Potter. It was found, however, to be a mixture of chrysophanolanthranol and the monomethyl ether of dehydroemodinanthranol, for, when subjected to a carefully regulated treatment with chromic acid, the anthranol alone was oxidised, and the resulting chrysophanol was then readily separated from the monomethyl ether of dehydroemodinanthranol. (Jowett and Potter found for "dichrysarobin methyl ether," C = 73·0; H = 4·9; CH_3 = 2·1 per cent.; m. p. 160°. A mixture of equal parts of chrysophanolanthranol and the monomethyl ether of dehydroemodinanthranol melts at about 170°, and requires C = 73·3; H = 4·8; CH_3 = 2·9 per cent.)

Constituent.	Percentage in sample *A*.	Percentage in sample *B*.	Percentage in sample *C*.
Chrysophanol Emodin monomethyl ether } *	6·3	7·2	8·9
Crude chrysophanolanthranol	about 26·0	about 46·0	about 62·0
Anthranol of emodin monomethyl ether	small amount	small amount	small amount
Monomethyl ether of dehydroemodinanthranol	41·1	13·4	17·7
Ararobinol	4·2	4·1	nil
Emodin	trace	nil	nil
Inseparable mixture of substances and amorphous matter	about 23·0	about 30·0	about 12·0

* About 3 or 4 parts of the former to 1 of the latter.

Now, the above-described mixture, on treatment with hydriodic acid, yields a product consisting of chrysophanolanthranol and emodinanthranol, and this product has the composition and properties assigned by Jowett and Potter to "dichrysarobin," as obtained by them after treatment of commercial chrysarobin with hydriodic acid. The specimens of "dichrysarobin" and its "methyl ether" prepared by the last-mentioned investigators being available to us, they were therefore re-examined in the light of more recent knowledge. It was thus found that when a solution of "dichrysarobin" in chloroform was shaken with 1 per cent. aqueous potassium hydroxide, emodinanthranol was removed and oxidised. On acidifying the red, alkaline liquid, emodin was obtained, its identity being confirmed by the preparation of its triacetyl derivative (m. p. 194°). The chloroform solution was then found to contain chrysophanolanthranol, which was extracted by 10 per cent. aqueous potassium hydroxide, when it was oxidised to chrysophanol. Similarly, when the specimen of "dichrysarobin methyl ether" was examined by the methods described in the present investigation, it was found to consist essentially of chrysophanolanthranol and the monomethyl ether of dehydroemodinanthranol, but it also contained small amounts of chrysophanol and emodin monomethyl ether.

The recent statement by Oesterle and Johann (*Arch. Pharm.*, 1910, **248**, 476) that chrysarobin contains emodin monomethyl ether has been confirmed, although the work of these authors did not prove that this compound existed as such in the natural material.

Summary and Conclusions.

From the results of the foregoing investigation it is seen that commercial chrysarobin is subject to considerable variation in the relative proportion of its constituents, some samples being even entirely devoid of certain compounds which occur in others. In the four products examined during the present work, chrysophanol, emodin monomethyl ether, the anthranols of these compounds,* and a new substance which proved to be the *monomethyl ether* of *dehydroemodinanthranol*, $C_{16}H_{12}O_4$, were invariably present. The original Araroba powder and two of the samples of chrysarobin also contained another new compound, *ararobinol*, $C_{23}H_{16}O_5$, whilst emodin was present in appreciable amount in the Araroba powder and to a small extent in one sample of chrysarobin. The Araroba powder also contained a small amount of a sugar which yielded *d*-phenylglucosazone and traces of the higher fatty acids, together with a product which appeared to be a hydrocarbon.

The "dichrysarobin" and "dichrysarobin methyl ether" of Jowett and Potter (Trans., 1902, **81**, 1575) have been found to be

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[*] No specific test for the presence of the anthranol of emodin monomethyl ether in the Araroba powder was made, but no doubt can be entertained of its presence.

mixtures of chrysophanolanthranol and emodinanthranol, and chrysophanolanthranol and the monomethyl ether of dehydroemodinanthranol respectively. The substance, $C_{17}H_{14}O_4$, obtained by Jowett and Potter (*loc. cit.*) could not be isolated from any of the products examined by the present authors.

In view of the variable nature of chrysarobin it is obviously fallacious to demand that it should fulfil exact requirements regarding its solubility, etc., as is done by some national pharmacopœias, notably that of the United States; moreover, the tests given by the last-mentioned work for distinguishing commercial chrysarobin from "chrysophanic acid" are of no value, for "chrysophanic acid" does not yield the reactions there attributed to it, and, furthermore, it is invariably a constituent of chrysarobin. The general characters of commercial chrysarobin, such as are described by the British Pharmacopœia, should be sufficient for the control of the purity of the product.

There is no definite knowledge as to which constituent or constituents of commercial chrysarobin its medicinal value is to be attributed. The active constituent has generally been presumed to be chrysophanolanthranol, but there appears to be a lack of evidence to support this view, especially as the artificially prepared anthranol has been stated not to exhibit the action of the natural drug. The valuable constituent may therefore be one of the new compounds described in the present communication.

The physiological action of chrysarobin is known to be very variable (compare *Pharm. J.*, 1911, [iv], **87**, 630), and this is doubtless attributable to the differences in the composition of the drug, such as are shown in the present communication to occur. It is not easy to see, however, how a more uniform product could be obtained from the chrysarobin at present found in commerce, since it is a difficult and most tedious process to ascertain even the approximate composition of a sample of the product in question. It would nevertheless appear significant that the differences observed between the three samples examined by the present authors are, to a great extent, such as would be caused by the employment of different methods for the extraction of the original Araroba powder, or, more particularly, by the varying degrees of completeness with which the extraction had been conducted. It is probable, therefore, that commercial chrysarobin would be of much more uniform composition if a definite solvent could be adopted for the extraction of the Araroba powder, and the extraction always made complete.

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